

In the Claims

1. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

- a) obtaining haplotypes for all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining haplotypes for all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups ~~using a binary code to generate a binary mask array, coding all haplotypes with a binary mask array and grouping identical genotypes within said array prior to performing haplotype frequency estimations;~~
- d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of step (a) and step (b) to determine the probability that the groups of step (a) and step (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and

- e) outputting the results of said analyzing to a printer or display.

2-3. (Canceled)

4. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising one or more electronically connected computers, an input device, an output device and:

(a) first instructions for identifying the haplotypes of all individuals in each of said at least two groups of individuals, that group identical genotypes and that code all haplotypes into a binary mask array using a binary code to generate a binary mask array;

(b) second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(c) third instructions for determining the sum of separate likelihoods that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(d) fourth instructions for determining the difference of said sum and said combined likelihood; and

(e) fifth instructions for determining the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (b) to determine the probability that the groups do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and

(f) sixth instructions that output the result of said fifth instructions to a printer or display
~~wherein said system comprises one or more electronically connected computers~~
~~executing said instructions and outputting the results obtained by execution of said instructions to a printer or display.~~

5-6. (Canceled)

7. (Currently Amended) A programmed storage device comprising instructions stored on said programmed storage device that when executed perform a method comprising:

(a) identifying the haplotypes of all individuals in at least two groups, coding all haplotypes with binary mask arrays and grouping identical genotypes within said arrays prior to performing

haplotype frequency estimations and determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately; and

(b) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (a) to determine the probability that the groups of (a) do not come from the same distribution of haplotypes, wherein said programmed storage device is a computer-readable medium selected from the group consisting of compact disks (CDs), floppy disks, hard-drives, magneto-optical drives, tape drives, zip drives, punch cards, Read Only Memory (ROM), Random Access Memory (RAM), and memory devices.

8-39. (Canceled)

40. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

- a) obtaining haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups, coding all haplotypes with a binary mask array and grouping identical genotypes within the array prior to performing haplotype frequency estimations~~identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;~~
- d) calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype;
- e) analyzing the haplotypes of said at least two groups of individuals to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of step (a) and step (b) to determine the probability that the groups of step (a) and step (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and

f) outputting the results of said analyzing to a printer or display.

41. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

a) obtaining haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;

b) obtaining haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;

c) identifying the haplotypes of all individuals in each of said at least two groups, coding all haplotypes with a binary mask array and grouping identical genotypes within the array prior to performing haplotype frequency estimations~~identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;~~

d) assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype;

e) analyzing the haplotypes of said at least two groups of individuals to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of step (a) and step (b) to determine the probability that the groups of step (a) and step (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and

f) outputting the results of said analyzing to a printer or display.

42-45. (Canceled)

46. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising one or more electronically connected computers, an input device, an output device and:

~~an input device and:~~

(a) first instructions for identifying the haplotypes of all individuals in each of said at least two groups of individuals, that group identical genotypes and that code all haplotypes into a binary mask array ~~using a binary code to generate a binary mask array;~~

(b) second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(c) third instructions for determining the sum of separate likelihoods that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(d) fourth instructions for determining the difference of said sum and said combined likelihood; and

(e) fifth instructions for calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype; and

(f) sixth instructions for determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (b) to determine the probability that the groups of (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and

(f) sixth instructions that output the result of said fifth instructions to a printer or display
~~wherein said system comprises one or more electronically connected computers executing said instructions and outputting the results obtained by execution of said instructions to a printer or display.~~

47. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising one or more electronically connected computers, an input device, an output device~~an input device~~ and:

first instructions for identifying the haplotypes of all individuals in each of said at least two groups of individuals, that group identical genotypes and that code all haplotypes into a binary mask array~~using a binary code to generate a binary mask array;~~

second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

third instructions for determining the sum of the separate likelihoods that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

fourth instructions for determining the difference of said sum and said combined likelihood; and

fifth instructions for calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype; and

sixth instructions for determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (b) to determine the probability that the groups of (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and

(f) sixth instructions that output the result of said fifth instructions to a printer or display
~~wherein said system comprises one or more electronically connected computers executing said instructions and outputting the results obtained by execution of said instructions to a printer or display.~~

48. (Currently Amended) A programmed storage device comprising instructions stored on said programmed storage device that when executed perform a method comprising:

(a) coding all haplotypes inputted by a user for the individuals in an affected group exhibiting a phenotype, the individuals in an unaffected group not exhibiting said phenotype and the individuals in another group with binary mask arrays and grouping identical genotypes binary mask arrays that represent a particular haplotype prior to performing haplotype frequency estimations;

(ba) determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

(cb) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (a) to determine the probability that the groups do not come from the same distribution of haplotypes; and

(de) calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype,

wherein said programmed storage device is a computer-readable medium selected from the group consisting of compact disks (CDs), floppy disks, hard-drives, magneto-optical drives, tape drives, zip drives, punch cards, Read Only Memory (ROM), Random Access Memory (RAM), and memory devices.

49. (Currently Amended) A programmed storage device comprising instructions stored on said programmed storage device that when executed perform a method comprising:

(a) coding all haplotypes inputted by a user for the individuals in an affected group exhibiting a phenotype, the individuals in an unaffected group not exhibiting said phenotype and the individuals in another group with binary mask arrays and grouping identical genotypes binary mask arrays that represent a particular haplotype prior to performing haplotype frequency estimations;

(ab) determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

(cb) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups of (a) to determine the probability that the groups do not come from the same distribution of haplotypes; and

(de) calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype, wherein said programmed storage device is a computer-readable medium selected from the group consisting of compact disks (CDs), floppy disks, hard-drives, magneto-optical drives, tape drives, zip drives, punch cards, Read Only Memory (ROM), Random Access Memory (RAM), and memory devices.

50. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

a) obtaining haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;

- b) obtaining haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups, coding all haplotypes with a binary mask array and grouping identical genotypes within the array prior to performing haplotype frequency estimations~~identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;~~
- d) using said binary mask array for analyzing the haplotypes of said at least two groups of individuals comprising the steps of:
 - 1) determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;
 - 2) determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;
 - 3) determining the difference of said sum and said combined likelihood; and
 - 4) determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (d)(1) and (d)(2) to determine the probability that the groups of (d)(1) and (d)(2) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance; and
- e) outputting the results of said analyzing to a printer or display.